ORIGINAL ARTICLE

Malignancy in multinodular goiter: analysis of trends

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Abstract:
Objective: To know the incidence of malignancy in multinodular goiter and analyze trends of its occurrence with respect to age and gender
Study Design: Descriptive cross-sectional study
Place and duration of study: Surgical Ward 25 of Endocrine and General surgery, Jinnah Postgraduate Medical Center, Karachi. This study carried out from 1st September 2017 to 30th March 2019.
Material and Methods: 122-patients with simple multinodular goiter were included in this study. Patients with toxic multinodular goiter (MNG), thyroid malignancy, recurrent thyroid disease and MNG below 12 years of age were excluded from this study. All patients who met study criteria underwent total thyroidectomy. Results are described as frequency, percentages and mean.
Results: 122-patients of multinodular goiter underwent total thyroidectomy, out of which 101 (82.78%) were benign and 21 (17.2%) were found to be malignant. Out of the 21 malignant biopsies, 17 (13.9%) were papillary thyroid cancer and 4 (3.27%) were follicular thyroid cancer. Of the 122 patients operated upon, 18 (14.75%) were below 30 years, 81 (66.39%) were between 30 to 50 years and 22 (18%) patients were above 50 years of age. MNG remained common in women as of the 122 patients 102 (83.6%) cases were female and 20 (16.39%) were male.
Conclusion: Multinodular goiter remains common in middle age females but malignancy was found to be more common in male multinodular goiter (7 out of 20 MNGs). The female to male ratio of MNG was found to be 5.1:1 whereas for malignancy this ratio was 2:1. Papillary cancer of thyroid was more common than the follicular variety. Thus, the authors conclude that MNG carries a risk of malignancy which should not be under-valued, and should be included in surveillance program.

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Introduction:
Multinodular goiter (MNG) is defined as an enlarged thyroid gland with multiple nodules and occurs in up to 4% of the population in iodine-sufficient countries, and its frequency increases with age.[1] Ultrasound helps in identifying dominant and suspicious nodule in a multinodular goiter which is amenable to cytological examination before undertaking any surgical intervention. In most of the cases patients with MNG present with the complain of neck swelling, other presenting symptoms include difficulty in swallowing, difficulty in breathing on lying down, hoarseness of voice due to a huge goiter pressing upon the recurrent laryngeal nerve or cosmetic concerns.[1,2] In most of the cases patients with multinodular goiter are euthyroid, however hypo or hyperthyroid states can exist with MNG.

Table-1: TRENDS in malignant MNGs (n= 21)

Age distribution	**Frequency + %**
< 30 years	5 (23.8%)
30-50 years	16 (66%)
>50 years	2 (9.5%)

Table-2: The female to male ratio of MNG was found to be 5.1:1 whereas for malignancy this ratio was 2:1.

Female	14 (66.6%)
Male	7 (33.3%)

The female to male ratio of MNG was found to be 5.1:1 whereas for malignancy this ratio was 2:1.

Multinodular goiters have historically been thought of as a benign condition with a low risk of associated malignancy however, recent studies have suggested that the incidence of malignancy in patients with MNG approaches that of patients with a solitary thyroid nodule.[2] Pre-operative diagnosis of thyroid cancer is commonly done through fine-needle aspiration (FNA). While it remains one of the best pre-operative methods of determining nodule malignancy, large studies have found FNAC to be non-diagnostic in up to 25% of the cases.[2] It is difficult to adequately evaluate a goiter containing multiple nodules because sampling every nodule is not practical and also creates challenges in following individual nodules for growth overtime, which is an additional factor that is used to gauge the suspicion for malignancy.[2]

Currently, the procedure of choice for bilateral MNG is total thyroidectomy (TT) because a complete resection avoids further surgeries for incidental thyroid cancer (as diagnosed by final pathology results) or disease recurrence. However, permanent hypothyroidism is a concern for patients because it necessitates lifelong hormone replacement therapy (HRT).[1]

Thyroid carcinoma is the most common endocrine cancer accounting for 92% of cancers of endocrine glands. Papillary thyroid cancer is the most common type, accounting for 85% of all cases of thyroid carcinoma.[4] The risk of malignancy in patients with MNG remains controversial. Previous research using ultrasound-guided fine-needle aspiration biopsy (FNAB) as a diagnostic tool reported that the prevalence of malignancy in patients with MNG was identical to that in patients with solitary nodular goiter, however, recent studies have reported that the risk of carcinoma in patients with MNG has been underestimated, and a prevalence in the range of 17% to 35% has been reported in surgical series.[1] Past studies have shown a correlation between thyroid cancer and female gender, middle-age, and single nodularity.[2] The purpose of this study is to report the gender and age distribution of MNG in our setup, the incidence of malignancy in simple MNG and its association with age and gender of the target population.

Material and Methods:

This cross-sectional descriptive study was conducted at Surgical Ward-25, Department of Endocrine and General Surgery, Jinnah Postgraduate Medical Center, Karachi, from 1st Sept 2017 to 31st Mar 2019. All patients who were diagnosed to have multinodular goiter on clinical and sonographic examination above the age of 12 years were included in this study. Patients were defined as having MNG if they had 2 or more nodules palpable clinically and on pre-operative ultrasound.[2] Patients having thyroid malignancy, toxicity, recurrent thyroid disease and MNG below 12 years were excluded from this study. We looked at the FNAC findings of patients prior to surgery to determine the efficacy of diagnostic testing. The final diagnosis was determined by final pathology of the surgical specimen. 122 patients of simple multinodular goiter were admitted from outpatient department. After taking written and informed consent data was collected on proforma.

Results:

Of the 122 patients enrolled in this study who underwent total thyroidectomy 102(83.6%) were females and 20 (16.39%) were males. Age distribution showed 18 (14.75%) patients to be below 30 years, 81(66.39%) between 30 to 50 years and 22(18%) above 50 years. Biopsies revealed 101(82.78%) cases to be benign and 21 (17.2%) were malignant in which 17(13.9%) were papillary carcinoma and 4(3.27%) were follicular carcinoma. Of the 21 malignant MNGs 14 (66.66%) were found to be in females

and 7 (33.33%) in males. Age distribution of the 21 malignant MNGs showed 5 (23.8%) patients to be below 30 years, 14 (66%) between 30 to 50 years and 2 (9.5%) above 50 years.

Discussion:

Dietary iodine deficiency remains the most common cause of multinodular goiters in our part of the world. With the increasing incidence of MNG an increase in the occurrence of thyroid malignancy has also been observed. Malignancy arising in the presence of MNG is usually of differentiated type with papillary variety of thyroid cancer being more common than follicular variety. Other malignancies of thyroid gland which can present like a MNG include medullary, anaplastic and lymphoma.

Thyroid ultrasonography (US) is useful to define the characters associated with malignancy, and to select in MNG those nodules which require FNA.[5] Ultrasound findings are increasingly used to help distinguish malignancy in patients with MNG. Features such as microcalcifications, hypoechoic appearance, irregular borders, and increased vascularity have all been associated with a higher risk of malignancy.[2]

FNAC has been found to have a high diagnostic accuracy. However, in the largest series, FNAC results are non-diagnostic or indeterminate in 20–25% of the cases, and false positive or false negative in 5% of the cases.[5] In few patients, a history of neck irradiation, nodule hardness or fixity to adjacent structures, and the presence of cervical adenopathy strongly suggest malignancy. But in the large majority of patients, the physician is left with more general clinical features such as sex, age, and solitary or multiple nodularity, the importance of which is reported in the literature with discrepant results.[5]

The results of this study indicate MNG to be commoner in female population (83.6%) as compared to males (16.39%). None of the patients in this study had the preoperative diagnosis of malignancy. Post-operative biopsy results revealed 21(17.2%) patients out of 122 to be harboring cancer in simple multinodular goiters. Papillary thyroid cancer remains the most common type of thyroid malignancy in our study as well (13.9%), the other variety being of follicular type (3.27%). This indicates that MNG in some cases may undergo dysplasia –neoplasia sequence and develop differentiated type of thyroid cancer. Another interesting finding as per the results of this study reveal that although the incidence of MNG is higher in females (83.6%) as compared to males (16.39%), the incidence of malignancy in male MNG (35%) was found to be greater than MNG in females (13.86%). Iodine deficiency as a cause of MNG is less frequent in males as compared to females, and it is conceivable that nodular thyroid disease in males is more often linked to the presence of neoplastic thyroid disease.[5] The age distribution trends were similar where both incidence of MNG (66.39%) and incidence of malignancy in MNG (66%) was found to be highest in 30- 50 years age group.

In another study by Nadeem K et al during 2 years period, total 141 patients of thyroid disease were seen in OPD out of which 98 patients had Multinodular goiter. Histopathology of these patients showed 10 malignancies & 88 benign. Most of the patients that turned out to be malignant belong to 41-50 years age group. 7 patients were female and 3 were male. Among the malignancies 50% were papillary, 30% were follicular, and 10% were anaplastic carcinoma & lymphomas each.[15]

On the contrary a study done by Lin YS et all concluded that multinodularity does not increase the risk of thyroid malignancy. However, patients with MNG who develop papillary carcinoma are at an increased risk of cancer multifocality.[1]

In another study conducted at Jinnah Postgraduate Medical Center in 2010, 397-patients of MNG were operated upon and only one patient was diagnosed to have papillary carcinoma on histopathological examination (0.25%).[16] Whereas, in this study 21 patients out of 122

MNGs were found to have thyroid cancer on final histopathology(17.2%).

The main limitation of this study was the lack of preoperative Fine Needle Aspiration Cytology (FNAC) which was not done as thyroid sonography was not suggestive of suspicious nodule in any case. This indicates the need of better sonographic examination so that cytology of any suspicious nodule can be performed.

Conclusion:
We conclude, like solitary thyroid nodules, multinodular goiter also carry an increased risk of having malignancy, risks being higher in male MNGs and between 30 to 50 years age group. 21 malignancy were found in 122 cases of MNGs.14 out of 102 MNG were found to be malignant in females and 7 out of 20 MNG in male have malignancy. The female to male ratio of MNG was found to be 5.1:1 whereas for malignancy this ratio was 2:1. Therefore, patients with multinodular goiter should be closely followed and must be included in surveillance programs. Papillary thyroid cancer remains the most common type of malignancy hence, total thyroidectomy remains the procedure of choice in patients with MNG.

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Role and contribution of authors:
Dr Fizzah Khalid, study design, manuscript writing and data collection

Dr Zahid Mehmood, Data collection, data analysis and literature search

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